```
=> d his

     (FILE 'HOME' ENTERED AT 16:42:36 ON 01 JUL 2003)

     FILE 'STNGUIDE' ENTERED AT 16:42:54 ON 01 JUL 2003

     FILE 'HOME' ENTERED AT 16:43:00 ON 01 JUL 2003

     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
     AT 16:43:54 ON 01 JUL 2003
L1           201 S PTEN (L) (GLUCOSE OR LONG? OR OBES?)
L2            77 DUP REM L1 (124 DUPLICATES REMOVED)
L3        213413 S HIS
L4            35 S L2 AND PHOSPHATASE?
L5            35 SORT L4 PY
L6            51 S L2 AND PY<=2001
L7            51 FOCUS L6 1-

     FILE 'STNGUIDE' ENTERED AT 16:49:31 ON 01 JUL 2003

     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
     AT 16:50:19 ON 01 JUL 2003
L8            26 S L2 NOT L6
L9            26 FOCUS L8 1-

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   13.32      46.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -0.65      -3.25

STN INTERNATIONAL LOGOFF AT 16:56:30 ON 01 JUL 2003
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L7 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2003 ACS
AN 2001:651567 CAPLUS
DN 135:205578
TI Antisense oligonucleotide inhibition of PTEN gene expression
SO U.S., 38 pp., Cont.-in-part of Appl. No. PCT/US99/29594.
CODEN: USXXAM
IN Monia, Brett P.; Cowsert, Lex M.; McKay, Robert
AB Antisense compds., compns. and methods are provided for modulating the expression of **PTEN**. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding **PTEN**. Methods of using these compds. for modulation of **PTEN** expression and for treatment of diseases and conditions assocd. with expression of **PTEN** are provided. Both phosphorothioated oligodeoxyribonucleotides and chimeric oligonucleotides contg. 2'-O-methoxyethylribonucleotides and 5-methylcytosine were tested, and up to 92% inhibition of **PTEN** gene was obsd. Such conditions include diabetes and hyperproliferative conditions. Methods for decreasing blood **glucose** levels, inhibiting PEPCK expression, decreasing blood insulin levels, decreasing insulin resistance, increasing insulin sensitivity, decreasing blood triglyceride levels or decreasing blood cholesterol levels in an animal using the compds. of the invention are also provided. The animal is preferably a human; also preferably the animal is a diabetic animal.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6284538	B1	20010904	US 2000-577902	20000524 <--
US 6020199	A	20000201	US 1999-358381	19990721 <--
WO 2001007457	A1	20010201	WO 1999-US29594	19991214 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001090341	A1	20011129	WO 2001-US16628	20010521 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1285061	A1	20030226	EP 2001-935740	20010521
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002058638	A1	20020516	US 2001-878582	20010611

L7 ANSWER 6 OF 51 MEDLINE
AN 2000400170 MEDLINE
TI Accelerated decline of blood **glucose** after intravenous **glucose** injection in a patient with Cowden disease having a heterozygous germline mutation of the **PTEN**/MMAC1 gene.
SO ANTICANCER RESEARCH, **(2000 May-Jun)** 20 (3B) 1901-4.
Journal code: 8102988. ISSN: 0250-7005.
AU Iida S; Ono A; Sayama K; Hamaguchi T; Fujii H; Nakajima H; Namba M; Hanafusa T; Matsuzawa Y; Moriwaki K
AB The **PTEN**/MMAC1, a putative tumor suppressor, has been demonstrated to dephosphorylate phosphatidylinositol 3, 4, 5-triphosphate, a key molecule involved in the insulin signaling pathway. The **PTEN** may act, therefore, as a negative regulator of insulin signaling. The patient with Cowden disease, having a heterozygous **PTEN**/MMAC1 gene mutation, a C to T substitution of a single base at codon 130, was suspected to have decreased amount of **PTEN** protein with phosphatase signature motif. We thought that the patient might be more sensitive to insulin than normal subjects. As expected, administration of a bolus of **glucose** resulted in a more rapid clearance of blood **glucose** than was observed in 5 control subjects, indicating the presence of insulin hypersensitivity in the patient. The euglycemic hyperinsulinemic clamp study provided additional evidence.

L7 ANSWER 8 OF 51 MEDLINE
AN 1999307426 MEDLINE
TI The **PTEN** tumor suppressor homolog in Caenorhabditis elegans regulates **longevity** and dauer formation in an insulin receptor-like signaling pathway.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1999 Jun 22)** 96 (13) 7427-32.
Journal code: 7505876. ISSN: 0027-8424.
AU Mihaylova V T; Borland C Z; Manjarrez L; Stern M J; Sun H
AB Inactivation of the tumor suppressor **PTEN** gene is found in a variety of human cancers and in cancer predisposition syndromes. Recently, **PTEN** protein has been shown to possess phosphatase activity on phosphatidylinositol 3,4,5-trisphosphate, a product of phosphatidylinositol 3-kinase. We have identified a homolog of **PTEN** in Caenorhabditis elegans and have found that it corresponds to the daf-18 gene, which had been defined by a single, phenotypically weak allele, daf-18(e1375). By analyzing an allele, daf-18(nr2037), which bears a deletion of the catalytic portion of CePTEN/DAF-18, we have shown that mutation in daf-18 can completely suppress the dauer-constitutive phenotype caused by inactivation of daf-2 or age-1, which encode an insulin receptor-like molecule and the catalytic subunit of phosphatidylinositol 3-kinase, respectively. In addition, daf-18(nr2037) dramatically shortens lifespan, both in a wild-type background and in a daf-2 mutant background that normally prolongs lifespan. The lifespan in a daf-18(nr2037) mutant can be restored to essentially that of wild type when combined with a daf-2 mutation. Our studies provide genetic evidence that, in C. elegans, the **PTEN** homolog DAF-18 functions as a negative regulator of the DAF-2 and AGE-1 signaling pathway, consistent with the notion that DAF-18 acts a phosphatidylinositol 3,4,5-trisphosphate phosphatase in vivo. Furthermore, our studies have uncovered a **longevity**-promoting activity of the **PTEN** homolog in C. elegans.

L9 ANSWER 6 OF 26 MEDLINE
AN 2002334115 MEDLINE
TI Negative feedback regulation of the tumor suppressor PTEN by phosphoinositide-induced serine phosphorylation.
SO JOURNAL OF IMMUNOLOGY, (2002 Jul 1) 169 (1) 286-91.
Journal code: 2985117R. ISSN: 0022-1767.
AU Birle Diana; Bottini Nunzio; Williams Scott; Huynh Huong; deBelle Ian; Adamson Eileen; Mustelin Tomas
AB The **PTEN** tumor suppressor phosphatase directly counteracts the multiple functions of phosphatidylinositol 3-kinase by removing phosphate from the D3 position of inositol phospholipids. Like many lymphomas and leukemias, the Jurkat T cell line lacks **PTEN** protein due to frame-shift mutations in both **PTEN** alleles and therefore survives in **long**-term cell culture. We report that **PTEN** reintroduced into Jurkat was highly phosphorylated on serines 380 and 385 in its C terminus, particularly the former site. Phosphate was also detected at Ser(380) in **PTEN** in untransformed human T cells. Treatments that reduced the levels of D3-phospholipids in the cells resulted in reduced phosphorylation and accelerated degradation of **PTEN**. In contrast, expression of inactive **PTEN**-C124G or coexpression of a constitutively active protein kinase B led to increased phosphorylation and slower degradation of **PTEN**. These results suggest that **PTEN** normally is subjected to a feedback mechanism of regulation aimed at maintaining homeostatic levels of D3-phosphoinositides, which are crucial for T cell survival and activation.

L9 ANSWER 3 OF 26 MEDLINE
AN 2002184354 MEDLINE
TI Specific inhibition of PTEN expression reverses hyperglycemia in diabetic mice.
SO DIABETES, (2002 Apr) 51 (4) 1028-34.
Journal code: 0372763. ISSN: 0012-1797.
AU Butler Madeline; McKay Robert A; Popoff Ian J; Gaarde William A; Witchell Donna; Murray Susan F; Dean Nicholas M; Bhanot Sanjay; Monia Brett P
AB Signaling through the phosphatidylinositol 3'-kinase (PI3K) pathway is crucial for metabolic responses to insulin, and defects in PI3K signaling have been demonstrated in type 2 diabetes. **PTEN** (MMAC1) is a lipid/protein phosphatase that can negatively regulate the PI3K pathway by dephosphorylating phosphatidylinositol (3,4,5)-triphosphate, but it is unclear whether **PTEN** is physiologically relevant to insulin signaling in vivo. We employed an antisense oligonucleotide (ASO) strategy in an effort to specifically inhibit the expression of **PTEN**. Transfection of cells in culture with ASO targeting **PTEN** reduced **PTEN** mRNA and protein levels and increased insulin-stimulated Akt phosphorylation in alpha-mouse liver-12 (AML12) cells. Systemic administration of **PTEN** ASO once a week in mice suppressed **PTEN** mRNA and protein expression in liver and fat by up to 90 and 75%, respectively, and normalized blood **glucose** concentrations in db/db and ob/ob mice. Inhibition of **PTEN** expression also dramatically reduced insulin concentrations in ob/ob mice, improved the performance of db/db mice during insulin tolerance tests, and increased Akt phosphorylation in liver in response to insulin. These results suggest that **PTEN** plays a significant role in regulating **glucose** metabolism in vivo by negatively regulating insulin signaling.